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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,212	05/30/2008	Ann Margaret Dyer	10774-88US ARCCX/P32619US	1191

570 7590 01/08/2010

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EXAMINER	
BROWE, DAVID	
ART UNIT	**PAPER NUMBER**
1616	

NOTIFICATION DATE	DELIVERY MODE
01/08/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomail@panitchlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,212	DYER ET AL.	
	Examiner	Art Unit	
	DAVID M. BROWE	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *24-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *May 30, 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-35 are pending.

Foreign Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 0403938.4, filed in the United Kingdom on February 21, 2004.

Domestic Benefit

Applicants claim for the benefit of prior-filed International application PCT/GB05/00592, filed February 18, 2005 under 35 U.S.C. 365(c) is acknowledged.

Election/Restriction

Applicant's election with traverse of Group I, Claims 1-23 in the telephone interview on December 10, 2009 is acknowledged.

Claims 24-35 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the telephone interview on December 10, 2009.

Specification

The disclosure is objected to for failing to comply with 37 CFR 1.77(b).

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenite *et al.* (U.S. Patent No. 6,344,488), in view of Dunn *et al.* (U.S. Patent No. 5,702,716).

Applicant Claims

Applicants claim a composition comprising: a) chitosan, or a derivative or salt thereof, b) a polyol-phosphate or sugar-phosphate salt, c) a plasticizer, and d) a therapeutic agent. The composition can take the form of an aqueous solution or suspension; has a viscosity of 150 cp or less at 25ºC; and forms a gel at 30°C or greater, with a gelation time of 15 minutes or less at 30-40ºC. The chitosan, or derivative or salt thereof, has a molecular weight of 4,000 Da. or greater, particularly 50,000-300,000 Da; a degree of deacetylation of 40% or greater, particularly 70-90%; comprises from 0.25-3.0% to 0.45-1.5% w/v of the composition; and can be a chitosan

base or derivative formed by bonding of acyl or alkyl groups with the hydroxyl groups of the chitosan or a nitrate, phosphate, sulphate, citrate, hydrochloride, glutamate, lactate, or acetate salt of chitosan. The polyol-phosphate or sugar-phosphate salt is β-glycerophosphate disodium; and comprises from 0.25-3.0% to 0.75-2.0% w/v of the composition. The plasticizer is triethyl citrate; and comprises from 0.05-5.0% to 0.2-1.0% w/v of the composition. The therapeutic agent is present in solution or suspension; is a polar drug, a polypeptide, a gene or a gene construct, insulin, calcitonin, leuprolide, luteinizing hormone releasing hormone, growth hormone or a growth hormone releasing factor, naratriptan, sumatripan, zolmitriptan, rizatriptan, eletriptan, frovatriptan, alnitidan, avitriptan, almotriptan, apomorphine, sildenafil, alprostadil, diamorphine, hydromorphine, buprenorphine, fentanyl, oxycodone, codeine, morphine, or morphine-6-glucuronide. The composition further comprises 0.01-0.2% w/v ascorbic acid.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Chenite *et al.* disclose a composition comprising: a) chitosan, or a derivative or salt thereof, b) a polyol-phosphate or sugar-phosphate salt, and c) a therapeutic agent (Col. 3, lns. 5-8, 14-25, 62-64; Col. 4, lns. 5-6, 30-31; Col. 5, lns. 65-66). The composition can take the form of an aqueous solution or suspension; and rapidly forms a gel at 30°C or greater (Col. 4, lns. 40-44; Col. 6, lns. 1-3; Col. 10, lns. 5-9; Col. 11, lns. 17-20, 28-31). The chitosan, or derivative or salt thereof, has a molecular weight of 4,000 Da. or greater, particularly 50,000-300,000 Da; comprises from 0.25-3.0% to 0.45-1.5% w/v of the composition; and can be a chitosan base or derivative formed by bonding of acyl or alkyl groups with the hydroxyl groups of the chitosan or a nitrate,

phosphate, sulphate, citrate, hydrochloride, glutamate, lactate, or acetate salt of chitosan (Col. 3, lns. 16-17; Col. 4, lns. 45-46; Col. 7, lns. 7-10). The chitosan deacetylation degree and molecular weight employed, and the solution pH all greatly influence the solution properties, such as viscosity, as well as the gelation time at a particular temperature, and can be adjusted as desired through routine optimization (Col. 7, lns. 4-6, Col. 9, lns. 11-55; Col. 12, lns. 22-25, 29-33). The polyol-phosphate or sugar-phosphate salt is β-glycerophosphate disodium; and comprises from 0.25-3.0% to 0.75-2.0% w/v of the composition (Col. 3, lns. 18-21, 50-56). The therapeutic agent is present in solution or suspension; is a polar drug, a polypeptide, a gene or a gene construct, insulin, calcitonin, leuprolide, luteinizing hormone releasing hormone, growth hormone or a growth hormone releasing factor, naratriptan, sumatripan, zolmitriptan, rizatriptan, eletriptan, frovatriptan, alnitidan, avitriptan, almotriptan, apomorphine, sildenafil, alprostadil, diamorphine, hydromorphine, buprenorphine, fentanyl, oxycodone, codeine, morphine, or morphine-6-glucuronide (Col. 13, lns. 9-22). The composition further comprises ascorbic acid (Col. 4, lns. 35-40)

Dunn *et al.* disclose a composition comprising: a) a thermoplastic polymer, b) a plasticizer, and c) a therapeutic agent (Col. 2, lns. 15-30). The composition can take the form of a solution or suspension, and can form a gel matrix *in situ* when implanted into a patient (Col. 1, lns. 65-67; Col. 2, lns. 8-10). The thermoplastic polymer is chitosan; and has a molecular weight preferably between 15,000-100,000 Da, corresponding to an inherent viscosity of 0.2-0.8 I.V. (Col. 4, lns. 19, 31; Col. 5, lns. 59-61; Col. 6, lns. 43-56). The plasticizer is triethyl citrate; and comprises from 0.05-5.0% to 0.2-1.0% w/v of

the composition (Col. 8, lns. 19, 26, 31, 43-53). The therapeutic agent is present in solution or suspension; is a polar drug, a polypeptide, a gene or a gene construct, insulin, calcitonin, leuprolide, luteinizing hormone releasing hormone, growth hormone or a growth hormone releasing factor, naratriptan, sumatripan, zolmitriptan, rizatriptan, eletriptan, frovatriptan, alnitidan, avitriptan, almotriptan, apomorphine, sildenafil, alprostadil, diamorphine, hydromorphine, buprenorphine, fentanyl, oxycodone, codeine, morphine, or morphine-6-glucuronide (Col. 10, lns. 1-67; Col. 11, lns. 1-24).

Ascertainment of the Difference Between the Scope of the Prior Art and the Claims (MPEP §2141.012)

Chenite *et al.* disclose a composition comprising: a) chitosan, or a derivative or salt thereof, b) a polyol-phosphate or sugar-phosphate salt, and c) a therapeutic agent, which can be inserted into a tissue or body cavity and function as a therapeutic agent delivery system. Chenite *et al.*, however, do not explicitly disclose the incorporation of a plasticizer into the composition. This deficiency is cured by Dunn *et al.*, who teach that such a composition can advantageously include a plasticizer.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the present invention to combine the teachings of Chenite *et al.* and Dunn *et al.* to arrive at a composition comprising: a) chitosan, or a derivative or salt thereof, b) a polyol-phosphate or sugar-phosphate salt, c) a plasticizer, and d) a therapeutic agent; which can be inserted into a tissue or body cavity and employed as a therapeutic agent

delivery system. Dunn *et al.* disclose that plasticizers provide significantly improved control to the sustained-release character of the chitosan therapeutic agent delivery system by causing the formation of a heretofore unknown distinctive macromolecular structure within the skin and core of the implant as the implant is formed (Col. 3, lns. 50-57; Col. 7, lns. 8-11, 16, 59-63). One of ordinary skill in the art, therefore, would be motivated to employ a pharmaceutically acceptable plasticizer, such as triethyl citrate, in the composition of Chenite *et al.*, with the reasonable expectation that the plasticizer will successfully provide the means to fine-tune and significantly improve control of the desired therapeutic agent release rate of the composition when implanted in a tissue or body cavity.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID M. BROWE whose telephone number is 571-270-1320. The examiner can normally be reached on Monday-Friday 7:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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